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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/661,696 | 09/14/2000 | Tina Meinertz Andersen | 6028.200-US | 8978 |

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| EXAMINER | |
|---|---|
| MOHAMED, ABDEL A | |
| ART UNIT | PAPER NUMBER |
| 1653 | |

DATE MAILED: 05/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/661,696 | ANDERSEN, TINA MEINERTZ | |
| | Examiner | Art Unit | |
| | Abdel A. Mohamed | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5,7,9-12 and 14-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7-11 and 26-52* is/are allowed.

6)☒ Claim(s) *1-5, 12 and 14-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

## ACKNOWLEGMENT OF THE AMENDMENT, REMARKS, CLAIM OFPRIORITY, STATUS OF THE APPLICATION AND CLAIMS

1. The amendment, remarks and executed substituted Declaration filed 3/4/04 claiming the benefit of Danish application PA 1999 01308 having a filing date of 9/16/99 are acknowledged, entered and considered. In view of Applicant's request, claims 8 and 13 have been canceled, claims 7 and 11 have been amended and claims 26-52 have been added. Claims 1-5, 7, 9-12 and 14-52 are now pending in the application.

The rejections under 35 U.S.C. 102(a) over WO 00/52142 and 35 U.S.C. 112, second paragraph are withdrawn in view of Applicant's submission an executed substituted Declaration claiming the benefit of Danish application PA 1999 01308 having a filing date of 9/16/99, amendment, remarks and cancellation of claims filed 3/4/04. Also, the rejections under 35 U.S.C. 102(b) and 103(a) for claims 7-11 over the prior art of record are withdrawn in view of Applicant's amendment and remarks. However, the rejection under 35 U.S.C. 102(b) for claims 1-5, 12 and 14-21 over WO 98/24883 is maintained for the reasons of record. Also, the rejection under 35 U.S.C. 103(a) for claims 1-5, 12, 14-25 over the prior art of record is maintained.

## CLAIMS REJECTION-35 U.S.C. § 102(b)

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 12, and 14-21 remain rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/24883.

WO 98/24883 discloses similarly a solid composition comprising meiosis activating substance (MAS) and an additive, wherein the additive and organic solvent are components when added to MAS provide a composition which can be used to prepare an aqueous containing MAS. With respect to the percentages content of water, organic solvent; the prior art does not disclose the above percentages content as claimed. However, the ranges disclosed in the prior art overlaps the claimed ranges. Further, it is the Examiner's position that since the above characteristics (i.e., percentages content) are in the properties and not in the structure of the claimed formulation/composition claimed, and as such it is inherent characteristics/properties of the prior art composition/formulation (See e.g., page 1, lines 5-31; pages 7-12, and the claims).

In regard to claim 12, which is directed to a device comprising a hollow containing the claimed composition, the prior art discloses the teaching of growing culture medium in a hollow container, and as such, the delivery system has a container or a hollow device containing the composition of MAS and additive for the purpose of growing cells thereof. Thus, the reference clearly discloses a composition comprising MAS and additive of protein or phosphoglyceride, which can be dissolved in the

aqueous medium in with a culturing system of a device containing a hollow composition thereof, and as such, anticipates claims 1-5, 12 and 14-21 as drafted.

3. **ARGUMENTS ARE NOT PERSUASIVE**

**CLAIMS REJECTION-35 U.S.C. § 102(b)**

The rejection of claims 1-5, 12 and 14-21 under 35 U.S.C. 102(b) as being anticipated by WO 98/24883.

Applicant's arguments filed 3/4/04 have been fully considered but they are not persuasive. Applicant has argued that WO 98/24883 relates to cell culture media and not to solid compositions comprising MAS and an additive such as a protein or phosphoglyceride. Whenever sterols are mentioned in WO 98/24883, it is always in the context of a solution or a medium (See e.g., page 5, lines 20-24). On page 6, lines 29-31, when specific amounts of cholesterol are mentioned it is in units of weight/vol and not vol/vol. Also, on page 6, lines 35-37, the reference disclose that "[T]he cholesterol or other sterol and the surfactant may be prepared in a concentrated solution for addition to a basal medium....". Thus, claims to a solid composition of MAS and additive such as a protein or phospholipid are not disclosed by WO 98/24883 is unpersuasive. Contrary to Applicant's arguments, independent claim 1 is broadly directed to a solid composition comprising MAS and an additive which is a protein or a phosphoglyceride. The MAS and the amount and/or kind or type of the protein or phosphoglyceride are not defined in the rejected claims, and as such reads on any MAS, protein and phosphoglyceride. The prior art clearly on pages 1-2 discloses the

advantages and disadvantages of using and/or adding additives, particularly proteins such as serum to grow cell cultures. Also, on page 8, lines 11-26, the reference indicates that it is necessary to add lipid solublizing materials such as serum, albumin or liposome to solublize certain basal media formulations which include one or more fatty acids such as linoleic acid. Thus, clearly showing the employment of protein or phosphoglyceride as an additive. Further, the prior art as acknowledged by Applicant above, clearly states on page 6, lines 35 to 38 that the cholesterol or other sterol and the surfactant may be prepared in a **concentrated solution** for addition to a basal medium to from a culture medium containing these materials in the required quantities. Thus, clearly disclosing a solid composition (concentrated solution) of MAS. With respect to Applicant's argument that when specific amounts of cholesterol are mentioned it is in units of weight/vol and not vol/vol is noted. However, this argument is not reflected on the limitations of the rejected claims because the specific amounts mentioned in the instantly claimed invention is not vol/vol as argued by Applicant, rather it is in weight/weight.

Applicant's assertion that there is no disclosure in WO 98/24883 of the specific MAS compounds that are mentioned in dependent claim 5 is noted. However, Applicant's attention is directed to page 2, lines 22 to 32 in the instant specification which discloses examples of the preferred MAS compounds as claimed in claim 5. These are known compounds disclosed in the prior art of WO 96/00235, 96/27658, 97/00884, 98/28323, 98/28323, 98/54965 and 98/55498, more specifically in claim 1 thereof.

In regard to Applicant's arguments that the specific compound 4,4-dimethyl-5αcholesta-8,14,24-triene-3β-ol and the limitations "higher than 99%" and "ratio of MAS to additive of at least 1:150") in claims 35-49 and 7, 9-11, 26-34 and 50-52, respectively are not disclosed in the prior art cited is noted. The rejections based on the above claims deemed to be moot in view of the withdrawal of the rejection.

With respect to the percentages content of water, organic solvent; the prior art does not disclose the above percentages content as claimed. However, the ranges disclosed in the prior art overlaps the claimed ranges. Further, since the above characteristics (i.e., percentages content) are in the properties and not in the structure of the claimed formulation/composition claimed, and as such it is inherent characteristics/properties of the prior art composition/formulation (See e.g., page 1, lines 5-31; pages 7-12, and the claims).

In regard to claim 12, which is directed to a device comprising a hollow containing the claimed composition, the prior art discloses the teaching of growing culture medium in a hollow container, and as such, the delivery system has a container or a hollow device containing the composition of MAS and additive for the purpose of growing cells thereof. Thus, the reference clearly discloses a composition comprising MAS and additive of which can be dissolved in the aqueous medium in with a culturing system of a device containing a hollow composition thereof, and as such anticipates claims 1-5, 12 and 14-21 as drafted.

**CLAIMS REJECTION-35 U.S.C. § 103(a)**

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 12, 14-25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/24883 taken with Wang et al., (Journal of Parenteral Science & Technology, Vol. 42, Supplement pp. 4-26, 1988).

The reference of WO 98/24883 discloses similarly a solid composition comprising meiosis activating substance (MAS) and an additive which is protein or a phosphoglyceride, wherein the additive and organic solvent are components when added to MAS provide a composition which can be used to prepare an aqueous containing MAS. With respect to the percentages content of water, organic solvent; the prior art does not disclose the above percentages content as claimed. However, the ranges disclosed in the prior art overlaps the claimed ranges. Further, the above characteristics (i.e., percentages content) are in the properties and not in the structure of the claimed formulation/composition claimed, and as such it is an expected characteristics/properties of the prior art composition/formulation (See e.g., page 1, lines 5-31; pages 7-12, and the claims).

In regard to claim 12, which is directed to a device comprising a hollow containing the claimed composition, the prior art discloses the teaching of growing culture medium in a hollow container, and as such, the delivery system has a container or a hollow device containing the composition of MAS and additive for the purpose of growing cells thereof. Thus, the reference clearly discloses a composition comprising MAS and additive of which can be dissolved in the aqueous medium in with a culturing system of a device containing a hollow composition thereof.

The prior art of WO 98/24883 differs from claims 1-5, 12, 14-25 in not teaching specifically the use of a protein additive, which is recombinant or native human serum albumin, or an additive, which is a phosphoglyceride. However, the primary reference clearly suggests the use of inorganic salts, amino acids, vitamins, and various other additives, which includes serum for maintaining the survival (i.e., viability, production of cell products and/or multiplication) of a basal cell culture medium (See e.g., page 1, lines 12-31). Thus, the above statements clearly suggest or motivate one of ordinary skill in the art the use of additives, which include serum for the purpose of maintaining the viability of cells in the basal media. Moreover, the secondary reference of Wang et al., clearly teaches the use of additives such as serum albumin as stabilizer by stating that serum albumin, regardless of its origin (rabbit, bovine or human), has been extensively cited in patents (e.g., Table I) and literature (Table Ia) as stabilizer for enzymes and other proteinaceous material. The reasons being for the choice of albumin over other proteins is its stability and solubility, and cites various mechanisms by which albumin acts as stabilizer (See e.g., pages S9 and S12). With respect of using

phosphoglyceride as stabilizer, on page S13 the reference discloses that fatty acids and phospholipids (which includes phosphoglyceride) or their derivative are well known stabilizers of proteins and examples of phospholipids are phosphatidyl choline, serine and ethanolamine as claimed in the in claims 1 and 24-25. Thus, the secondary reference teaches the use of additives, which are human serum albumin or phosphoglyceride.

Therefore, given the teachings of the secondary reference of Wang et al., one of ordinary skill in the art would have been motivated to adapt the above scheme of using additives which are proteins or phosphoglyceride for the intended purpose of stabilizing a solid composition comprising a meiosis activating substance, because such features of stabilizing any protein of interest by using the additives of the secondary reference, namely, serum albumin and phospholipid are known in the art. Hence, including such features into the solid composition comprising a meiosis activating substance of the primary reference in view of the secondary reference, would have been obvious to one having ordinary skill in the art to obtain the known and recognized functions and advantages thereof. Thus, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill the art would have been motivated at the time the invention was made to employ a solid composition comprising a meiosis activating substance and an additive which is a protein or a phosphoglyceride and a device formulation thereof, absent of sufficient objective factual evidence or unexpected results to the contrary.

**ARGUMENTS ARE NOT PERSUASIVE**

5. The rejection of claims 1-5, 12, 14-25 under 35 U.S.C. 103(a) as being unpatentable over WO 98/24883 taken with Wang et al., (Journal of Parenteral Science & Technology, Vol. 42, Supplement pp. 4-26, 1988).

Applicant has argued that the prior art of record either singularly or in combination does not teach 1) solid compositions comprising MAS and an additive such as a protein or phosphoglyceride; 2) the specific MAS compounds that are mentioned in dependent claim 5 nor the compound 4,4-dimethyl-5α-cholesta-8,14,24-triene-3β-ol which is the subject of added claims 35-49; and 3) the limitations "higher that 99%" or "ratio of MAS to additive of at least 1:150" in claims 7, 9-11, 26-34 and 50-52 is not persuasive. Contrary to Applicant's arguments, the Examiner has clearly indicated as discussed above that independent claim 1 is broadly directed to a solid composition comprising MAS and an additive which is a protein or a phosphoglyceride. The MAS and the amount and/or kind or type of the protein, except for the proteins of claims 22 and 23) or phosphoglyceride are not defined in the rejected claims, and as such reads on any MAS, protein and phosphoglyceride. The primary reference clearly on pages 1-2 discloses the advantages and disadvantages of using and/or adding additives, particularly proteins such as serum to grow cell cultures. Also, on page 8, lines 11-26, the reference indicates that it is necessary to add lipid solublizing materials such as serum, albumin or liposome to solublize certain basal media formulations which include one or more fatty acids such as linoleic acid. Thus, clearly showing the employment of protein or phosphoglyceride as an additive. Further, the primary reference as

acknowledged by Applicant above, clearly states on page 6, lines 35 to 38 that the cholesterol or other sterol and the surfactant may be prepared in a **concentrated solution** for addition to a basal medium to from a culture medium containing these materials in the required quantities. Thus, clearly disclosing a solid composition (concentrated solution) of MAS.

Applicant's assertion that there is no disclosure in WO 98/24883 of the specific MAS compounds that are mentioned in dependent claim 5 is noted. However, Applicant's attention is directed to page 2, lines 22 to 32 in the instant specification which discloses examples of the preferred MAS compounds as claimed in claim 5. These are known compounds disclosed in the prior art of WO 96/00235, 96/27658, 97/00884, 98/28323, 98/28323, 98/54965 and 98/55498, more specifically in claim 1 thereof.

In regard to Applicant's arguments that none of the prior art of record discloses the specific compound 4,4-dimethyl-5$\alpha$cholesta-8,14,24-triene-3$\beta$-ol and the limitations "higher than 99%" and "ratio of MAS to additive of at least 1:150") in claims 35-49 and 7, 9-11, 26-34 and 50-52, respectively is noted. However, the rejections based on the above claims deemed to be moot in view of the withdrawal of the rejection.

With respect to the percentages content of water, organic solvent; the primary reference does not disclose the above percentages content as claimed. However, the ranges disclosed in the prior art overlaps the claimed ranges. Further, since the above characteristics (i.e., percentages content) are in the properties and not in the structure of the claimed formulation/composition claimed, and as such it is inherent

characteristics/properties of the prior art composition/formulation (See e.g., page 1, lines 5-31; pages 7-12, and the claims).

In regard to claim 12, which is directed to a device comprising a hollow containing the claimed composition, the primary reference discloses the teaching of growing culture medium in a hollow container, and as such, the delivery system has a container or a hollow device containing the composition of MAS and additive for the purpose of growing cells thereof. Thus, the reference clearly discloses a composition comprising MAS and additive of which can be dissolved in the aqueous medium in with a culturing system of a device containing a hollow composition thereof.

With respect to recombinant or native human serum albumin, or an additive, which is a phosphoglyceride; the primary reference clearly suggests the use of inorganic salts, amino acids, vitamins, and various other additives, which includes serum for maintaining the survival (i.e., viability, production of cell products and/or multiplication) of a basal cell culture medium (See e.g., page 1, lines 12-31). Thus, the above statements clearly suggest or motivate one of ordinary skill in the art the use of additives, which include serum for the purpose of maintaining the viability of cells in the basal media. However, the secondary reference of Wang et al., clearly teaches the use of additives such as serum albumin as stabilizer by stating that serum albumin, regardless of its origin (rabbit, bovine or human), has been extensively cited in patents (e.g., Table I) and literature (Table Ia) as stabilizer for enzymes and other proteinaceous material. The reasons being for the choice of albumin over other proteins is its stability and solubility, and cites various mechanisms by which albumin acts as stabilizer (See

e.g., pages S9 and S12). With respect of using phosphoglyceride as stabilizer, on page S13 the reference discloses that fatty acids and phospholipids (which includes phosphoglyceride) or their derivative are well known stabilizers of proteins and examples of phospholipids are phosphatidyl choline, serine and ethanolamine as claimed in the in claims 1 and 24-25. Thus, the secondary reference teaches the use of additives, which are human serum albumin or phosphoglyceride.

Therefore, given the teachings of the secondary reference of Wang et al., one of ordinary skill in the art would have been motivated to adapt the above scheme of using additives which are proteins or phosphoglyceride for the intended purpose of stabilizing a solid composition comprising a meiosis activating substance, because such features of stabilizing any protein of interest by using the additives of the secondary reference, namely, serum albumin and phospholipid are known in the art. Hence, including such features into the solid composition comprising a meiosis activating substance of the primary reference in view of the secondary reference, would have been obvious to one having ordinary skill in the art to obtain the known and recognized functions and advantages thereof. Thus, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill the art would have been motivated at the time the invention was made to employ a solid composition comprising a meiosis activating substance and an additive which is a protein or a phosphoglyceride and a device formulation thereof as discussed above. Therefore, it is made obvious by the combined teachings of the prior art since the instantly claimed invention which falls within the scope of the combined teachings of the prior art method would have been *prima facie*

obvious from said prior art disclosure to a person of ordinary skill in the art because as held in host of cases including *Ex parte Harris*, 748 O.G. 586; *In re Rosselete*, 146 USPQ 183; *In re Burgess*, 149 USPQ 355 and as exemplified by *In re Best*, "the test of obviousness is not express suggestion of the claimed invention in any and all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them".

**ACTION IS FINAL**

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

**CONCLUSION AND FUTURE CORRESPONDANCE**

7. Claims 7-11 and 26-52 are allowed and claims 1-5, 12 and 14-25 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

AM Mohamed/AAM

May 14, 2004